Claims

We claim:

1. Use of a T-cadherin polypeptide as a target for screening candidate modulators for candidate drugs for the treatment of a disorder selected from the group consisting of a metabolic disorder, a gynecologic disorder, a chronic inflammatory disorder and a liver or renal disorder, wherein said candidate drug is a T-cadherin modulator.

2. The use of claim 1, wherein said candidate modulator is selected from the group consisting of natural ligands, small molecules, aptamers, antisense mRNAs, small interfering RNAs, soluble forms of T-cadherin and antibodies.

3. The use of claim 1 or 2, wherein said disorder is a metabolic disorder selected from the group consisting of obesity, type II diabetes, insulin resistance, hypercholesterolemia, hyperlipidemia, dyslipidemia and syndrome X.

4. The use of any of claims 1 to 3, wherein said disorder is obesity.

5. The use of any of claims 1 to 3, wherein said disorder is type II diabetes.

6. The use of any of claims 1 to 3, wherein said disorder is syndrome X.

7. The use of any of claims 1 to 6, wherein said modulator is an agonist.

8. The use of claim 7, wherein said candidate modulator is selected from the group consisting of a natural ligand, a small molecule and an aptamer.

9. The use of claim 1 or 2, wherein said disorder is a metabolic disorder selected from the group consisting of anorexia and cachexia.

10. The use of claim 1, 2 or 9, wherein said modulator is an antagonist.

11. The use of any of claim 1 to 10, wherein the activity of said T-cadherin polypeptide is assessed by measuring binding of said T-cadherin polypeptide to Acrp30.

12. The use of claim 11, wherein said Acrp30 is a hexameric species of Acrp30.

13. The use of claim 11, wherein said Acrp30 is a high molecular weight species of Acrp30.

14. Use of a modulator of a T-cadherin polypeptide for the preparation of a medicament for the treatment of a disorder selected from the group consisting of a metabolic disorder, a gynecologic disorder, a chronic inflammatory disorder and a liver or renal disorder.

15. The use of claim 14, wherein said disorder is a metabolic disorder selected from the group consisting of obesity, type II diabetes, insulin resistance, hypercholesterolemia, hyperlipidemia, dyslipidemia, syndrome X, anorexia and cachexia.

16. The use of claim 15, wherein said modulator is used in combination with a known drug for the treatment of said disorder.

17. The use of claim 15 or 16, wherein said disorder is a metabolic disorder selected from the group consisting of obesity, type II diabetes, insulin resistance, hypercholesterolemia, hyperlipidemia, dyslipidemia and syndrome X.

18. The use of claim 17, wherein said modulator is an agonist.

19. The use of claim 15 or 16, wherein said disorder is a metabolic disorder selected from the group consisting of anorexia and cachexia.

20. The use of claim 19, wherein said modulator is an antagonist.

21. Use of a T-cadherin polypeptide as a target for screening for natural binding partners, wherein said natural binding partner is a candidate drug for the treatment of a

disorder selected from the group consisting of a metabolic disorder, a gynecologic disorder, a chronic inflammatory disorder and a liver or renal disorder.

22. The use of claim 21, wherein said disorder is a metabolic disorder selected from the group consisting of obesity, type II diabetes, insulin resistance, hypercholesterolemia, hyperlipidemia, dyslipidemia, syndrome X, anorexia and cachexia.

23. The use of any of claims 1 to 22, wherein said T-cadherin polypeptide is a human T-cadherin.

24. The use of claim 23, wherein said T-cadherin polypeptide is selected from the group consisting of:

a) a polypeptide comprising SEQ ID NO: 1;
b) a polypeptide comprising amino acid 23 to 713 of SEQ ID NO: 1;
c) a polypeptide comprising amino acid 23 to 693 of SEQ ID NO: 1;
d) a polypeptide comprising amino acids 140 to 713 of SEQ ID NO: 1;
e) a polypeptide comprising amino acids 140 to 693 of SEQ ID NO: 1;
f) a mutein of any of (a) to (e), wherein the amino acid sequence has at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identity to at least one of the sequences in (a) to (e);
g) a mutein of any of (a) to (e) which is encoded by a nucleic acid which hybridizes to the complement of a DNA sequence encoding any of (a) to (e) under highly stringent conditions; and
h) a mutein of any of (a) to (e) wherein any changes in the amino acid sequence are conservative amino acid substitutions of the amino acid sequences in (a) to (e).

25. Use of a soluble form of T-cadherin as medicament.

26. Use of a soluble form of T-cadherin for the preparation of a medicament for the treatment of a disorder selected from the group consisting of a metabolic disorder, a gynecologic disorder, a chronic inflammatory disorder and a liver or renal disorder.

27. The use of claim 26, wherein said disorder is a metabolic disorder selected from the group consisting of obesity, type II diabetes, insulin resistance, hypercholesterolemia, hyperlipidemia, dyslipidemia, syndrome X, anorexia and cachexia.

28. The use of any of claims 25 to 27, wherein said soluble form of T-cadherin is a soluble form of a human T-cadherin.

29. The use of claim 28, wherein said soluble form is selected from the group consisting of:

a) a polypeptide consisting of amino acids 23 to 692 of SEQ ID NO: 1;
b) a polypeptide consisting of amino acids 23 to 692 of SEQ ID NO: 1;
c) a polypeptide consisting of a fragment of at least 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600 or 650 amino acids of (a) or (b);
d) a mutein of any of (a) to (c), wherein the amino acid sequence has at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identity to at least one of the sequences in (a) to (c);
e) a mutein of any of (a) to (c) which is encoded by a nucleic acid which hybridizes to the complement of a DNA sequence encoding any of (a) to (c) under highly stringent conditions; and
f) a mutein of any of (a) to (c) wherein any changes in the amino acid sequence are conservative amino acid substitutions of the amino acid sequences in (a) to (c).

30. A method of assessing the efficiency of a modulator of a T-cadherin polypeptide for the treatment of obesity, said method comprising administering said modulator to an animal model for obesity, wherein a determination that said modulator ameliorates a representative characteristic of obesity in said animal model indicates that said modulator is a drug for the treatment of obesity.

31. The method of claim 30, wherein said animal model is selected from the group consisting of a fa/fa rat, an ob/ob mouse, a db/db mouse, a leptin deficient mouse and a leptin-receptor deficient mouse.

32. The method of claim 30 or 31, wherein said representative characteristic is selected from the group consisting of the Body Mass Index (BMI), the body weight and the percentage of body fat.

33. The method of any of claim 30 to 32, wherein a reduction of 10% or more of the body weight indicates that said modulator is a drug for the treatment of obesity.

34. A method of assessing the efficiency of a modulator of a T-cadherin polypeptide for the treatment of type II diabetes, said method comprising administering said modulator to an animal model for type II diabetes, wherein a determination that said modulator ameliorates a representative characteristic of type II diabetes in said animal model indicates that said modulator is a drug for the treatment of type II diabetes.

35. The method of claim 34, wherein said animal model is selected from the group consisting of a C57/BLKsJ diabetic mouse, a KKA(y) mouse, a Nagoya-Shibata-Yasuda (NSY) mouse and a db/db mouse.

36. The method of claim 34 or 35, wherein said representative characteristic is selected from the group consisting of the fasting plasma glucose (FPG) level, the postprandial glucose level, the fructosamine and glycated hemoglobin (HbA1c) level, the total cholesterol level, the HDL cholesterol level, the LDL cholesterol level and the triglyceride level.

37. The method of any of claim 34 to 36, wherein said representative characteristic is the HbA1c level.

38. The method of claim 37, wherein a reduction in HbA1c levels of at least 0.5 % versus placebo indicates that said modulator is a drug for the treatment of type II diabetes.

39. The method of any of claim 30 to 38, wherein said modulator is an agonist.

40. The method of any of claim 30 to 39, wherein said T-cadherin polypeptide is a human T-cadherin.

41. The method of claim 40, wherein said T-cadherin polypeptide is selected from the group consisting of:

a) a polypeptide comprising SEQ ID NO: 1;

b) a polypeptide comprising amino acid 23 to 713 of SEQ ID NO: 1;

c) a polypeptide comprising amino acid 23 to 693 of SEQ ID NO: 1;

d) a polypeptide comprising amino acids 140 to 713 of SEQ ID NO: 1;

e) a polypeptide comprising amino acids 140 to 693 of SEQ ID NO: 1;

f) a mutein of any of (a) to (e), wherein the amino acid sequence has at least 80%, 90%, 95%, 96%, 97%, 98% or 99% identity to at least one of the sequences in (a) to (e);

g) a mutein of any of (a) to (e) which is encoded by a nucleic acid which hybridizes to the complement of a DNA sequence encoding any of (a) to (e) under highly stringent conditions; and

h) a mutein of any of (a) to (e) wherein any changes in the amino acid sequence are conservative amino acid substitutions of the amino acid sequences in (a) to (e).